

## REMARKS

Claims 1, 3-6 and 25 have been rejected under 35 USC 103 as allegedly unpatentable over Huang in view of Hoofnagle and Moody et al. Applicant respectfully traverses this rejection.

The Applicant has found that improved results are achieved with a combination therapy over using either  $\alpha$ -interferon alone or Thymosin  $\alpha$  alone. No one in the literature or otherwise has ever suggested using thymosin for the treatment of Hepatitis C. Also, no one in the literature or otherwise used or suggested the use of the two ingredients together at the time of the invention.

None of the cited references, whether taken alone or in combination suggest the combination of these two ingredients as a suitable and effective means for treating Hepatitis C.

The Examiner has suggested on page 3 of the office action that since both Hepatitis B and Hepatitis C cause liver disease and because both are viruses, one of ordinary skill in the art would conclude that a treatment for one virus would be effective against the treatment of the other virus. This statement simply is not supportable. A scientist experienced with Hepatitis B and Hepatitis C would not have made that conclusion because Hepatitis C is caused by an RNA virus and Hepatitis B is caused by a DNA virus (emphasis added). These two types of viruses operate differently in a host. For Hepatitis C, the injury is caused by the virus itself. For Hepatitis B, the injury is caused by the immunologic response to the virus.

Hepatitis C virus (HCV) core protein regulates cellular protooncogenes at the transcriptional level; this observation implicates core protein in the alteration of normal hepatocyte growth. There may be a possible mechanism for this viral protein in the pathogenesis of hepatocellular carcinoma in HCV- infected humans. Hepatitis C virus core protein cooperates with ras and transforms primary rat embryo fibroblasts to tumorigenic phenotype, RB Ray, LM Lagging, K Meyer and R Ray, J. Virol., Jul 1996, 4438-4443, Vol 70, No. 7

There are other differences between the two diseases as well. About 30% of persons with Hepatitis B show no symptoms. About 80% of persons with Hepatitis C show no symptoms. Hepatitis C is less likely than the other hepatitis viruses to cause

serious illness at first (only one-quarter of the people infected actually develop symptoms). There is a vaccine for preventing Hepatitis B that is available for all age groups that prevents hepatitis B virus infection (available since 1982). There is no vaccine for preventing hepatitis C. No generalized assumption would have been made by one of ordinary skill in the art that a vaccine that works for one type of Hepatitis would work for the other type and further, no generalized assumption could have been made at the time of the invention that a therapy that works for Hepatitis B would also work for Hepatitis C.

The Wikipedia website states as follows:

**Hepatitis** (plural **hepatitides**) implies injury to liver characterised by presence of inflammatory cells in the liver tissue. Etymologically from ancient Greek *hepar* (ήπαρ) or *hepato-* (ήπατο-) meaning 'liver' and suffix *-itis* denoting 'inflammation' (c.1727).

McKinley Health Center, Univ. of Illinois, Urbana-Champaign. 8.1.2007, website states:

Hepatitis is an inflammation of the liver caused by medications, alcohol, or a variety of other agents including the viruses that cause mumps, measles, herpes and infectious mononucleosis. However, when health professionals talk about viral hepatitis, they usually mean hepatitis caused by the hepatitis A, hepatitis B, or hepatitis C virus.

Although Hepatitis B virus and Hepatitis C virus affect the liver, so do a host of other viruses such as the viruses that cause the mumps, measles, herpes and infectious mononucleosis. It is respectfully submitted that the Examiner's argument that because both Hep B and Hep C are viruses that affect the liver, a treatment for one would work for the other cannot be supported. One would also have to speculate that the same treatment would work for mumps, measles, herpes and mononucleosis using such logic because they are all viruses that cause Hepatitis. Applicants respectfully submit that one of ordinary skill in the art at the time of the invention would not have made that assumption.

#### **Discussion of the References:**

**Huang et al.** is directed to a composition for treating Hepatitis B rather than Hepatitis C. Huang et al. combines  $\alpha$ -interferon and thymosin to treat Hepatitis B.

Huang et al. examines antigens and antibodies of HBV and HBcAg, DNAP, HBV-DNA. Huang, et al. is silent about Hepatitis C virus, antigens and antibodies. Huang, et al. is also careful not to speculate that its treatment for Hepatitis B would be useful for any other type of Hepatitis virus, other virus that attacks the liver or other disease forming viruses known to man.

As stated above, in Hepatitis B, the injury is caused by the immunologic response to the virus. Hepatitis C virus does not hurt the liver by the immunologic response to the virus. In Hepatitis C, the virus itself attacks the liver. Given the different modes of operation of the two types of viruses, it cannot be stated based on Huang, et al. that a therapy for one would be effective against the other.

The present composition claims require “an anti-Hepatitis C viral effective amount of at least one  $\alpha$ -interferon, said pharmaceutical dosage unit being capable of promoting *in vivo* inactivation of hepatitis C virus.” The present method claims call for treating Hepatitis C by administering to a mammal an anti-hepatitis C viral effective amount of at least one  $\alpha$ -interferon, concurrently or sequentially with administering a thymosin or thymosin fragment. Huang et al. does not indicate that thymosin is useful for treating Hepatitis C and, therefore, does not lead the artisan to the claims of the invention or any other RNA virus like Hepatitis C.

Therefore, the composition of Huang, et al. does not render obvious the present claims, especially when there is no motivation to use the claimed ingredients together to treat Hepatitis C.

**Hoofnagle, et al.** does not make up for the deficiencies of Huang, et al. Hoofnagle et al. discloses a composition containing only  $\alpha$ -interferon for treating Hepatitis C. There is no mention of the use of thymosin for treating Hepatitis C or the combination of  $\alpha$ -interferon with thymosin for treating Hepatitis C. There is no disclosure that a treatment for Hepatitis B would work for Hepatitis C or vice versa. There is no disclosure that Hepatitis C and Hepatitis B are similar viruses. There is also no suggestion of what the proper dosage unit of thymosin would be or what parameters would be useful to achieve the proper dosage unit of thymosin for the combination therapy of the claims. Although, Hoofnagle, et al. briefly discusses using *other antiviral agents or corticosteroids* in treating Hepatitis C in patients with suspected Hepatitis C

who have not responded to alpha interferon, Hoofnagle, et al. does not suggest using immune system potentiating agents for treating Hepatitis C (page 261, col 2, last paragraph). Without any motivation present in, Hoofnagle et al. to use an immune system potentiating agent such as thymosin, Hoofnagle, et al. would not have lead the skilled artisan to the present invention.

**Moody** is directed to compositions and methods for treating small cell and nonsmall cell lung cancers, not viruses, not Hepatitis C virus. Moody indicates that thymosin and interferon operates to treat the endogenous biochemical factors that regulate the growth of lung cancer cells. Moody has been cited to show that thymosin fragments have been identified to have “therapeutic significance.” “Therapeutic significance” does not establish a prima fascia case of obviousness in the present application’s claims.

There must be some motivation for (1) the use of thymosin with interferon and (2) this combination of thymosin with interferon for the treatment of Hepatitis C virus for Moody to be successfully combined with the other references. In this case, there is not. Not only is there no combined therapy in Moody for treating Hepatitis C virus, there is no use of a combined therapy for the treatment of any other viral entity.

Therefore, Moody does not add to the disclosures of the above two references in such a way that would have motivated one of ordinary skill in the art to try thymosin with  $\alpha$ -interferon to treat an RNA virus like Hepatitis C.

Applicant states that a doctor of ordinary skill in the art would not have automatically combined therapies of antiviral agents and immune potentiating agents for a particular disease without a great deal of experimentation because of the fear of side effects or the canceling of effectiveness or otherwise. It is respectfully submitted that the combination of Huang, et al., Hoofnagle, et al. and Moody would not have motivated one of ordinary skill in the art at the time of the invention to arrive at the present claims under 35 USC §103(a).

Reconsideration and allowance are respectfully requested.

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Respectfully submitted,



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